

Practitioner's Docket No. MPI00-452P1RM

U.S.S.N. 10/060,714

IN THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Original) A hybrid antibody molecule, comprising:
 - at least one light chain variable region comprising all three complementarity determining region (CDR's) from a donor immunoglobulin and a light chain variable region framework from an acceptor immunoglobulin; and
 - at least one heavy chain variable region selected from the group consisting of:
 - (a) a heavy chain variable region which is at least 95% identical to the heavy chain variable region of the donor immunoglobulin; and
 - (b) a heavy chain variable region from the donor immunoglobulin.
2. (Original) The hybrid antibody molecule of claim 1, wherein the acceptor immunoglobulin is a human immunoglobulin.
3. (Original) The hybrid antibody molecule of claim 1, wherein the heavy chain variable region is a fully rodent immunoglobulin sequence.
4. (Original) The hybrid antibody molecule of claim 1, wherein the light chain variable region is a humanized or a CDR-grafted immunoglobulin chain.
5. (Original) The hybrid antibody molecule of claim 1, wherein the heavy chain variable region is a chimeric chain.
6. (Original) The hybrid antibody molecule of claim 1, which binds to an antigen with an affinity constant between 10^8 M^{-1} and 10^{10} M^{-1} .
7. (Original) The hybrid antibody molecule of claim 1, which comprises two heavy chains and two light chains.

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8. (Original) The hybrid antibody molecule of claim 1, which comprises a constant region selected from the group consisting of kappa, lambda, alpha, gamma, delta, epsilon and mu constant region genes.
9. (Original) The hybrid antibody molecule of claim 8, wherein the heavy chain or the light chain constant region is from human origin.
10. (Original) The hybrid antibody molecule of claim 8, wherein the heavy chain constant region is of a human isotype selected from the group consisting of IgG1, IgG2, IgG3, IgG4, IgM, IgA1, IgA2, IgAsec, IgD, and IgE.
11. (Original) The hybrid antibody molecule of claim 8, wherein the heavy chain constant region is of human isotype IgG1.
12. (Original) The hybrid antibody of claim 1, which binds to an immune cell antigen.
13. (Original) The hybrid antibody molecule of claim 12, wherein the immune cell antigen is selected from the group consisting of CD1, CD2, CD3, CD4, CD5, CD8, CD18, CD20, CD23, CD40L, CD80, and CD86.
14. (Original) The hybrid antibody molecule of claim 12, wherein the immune cell antigen is a chemokine receptor selected from the group consisting of a CXC chemokine receptor and a CC chemokine receptor.
15. (Original) The hybrid antibody molecule of claim 14, wherein the CC chemokine receptor is selected from the group consisting of a CCR1, CCR2A, CCR2B, CCR3, CCR4, CCR5, CCR6, CCR7, CCR8 and CCR9.
16. (Original) The hybrid antibody molecule of claim 1, which binds to a tumor antigen.

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17. (Original) The hybrid antibody molecule of claim 16, wherein the tumor antigen is selected from the group consisting of EGFR, Her2/neu, HELP, GCC, PSMA, PSA, CD66-c, prostasin, TMPRSS3, TADG 12 and TADG 15.
18. (Original) A hybrid antibody molecule, comprising at least one humanized or CDR-grafted light chain variable region and at least one chimeric heavy chain.
19. (Original) An anti-CD3 hybrid antibody molecule, comprising:
at least one light chain variable region comprising all three CDR's from a first donor species immunoglobulin and a light chain variable region framework from an acceptor immunoglobulin; and
at least one heavy chain variable region selected from the group consisting of:
(a) a heavy chain variable region at least 95% identical to the heavy chain variable region of the donor immunoglobulin; and
(b) a heavy chain variable region from the donor immunoglobulin.
20. (Original) The anti-CD3 antibody molecule of claim 19, wherein the donor is a rat or a mouse.
21. (Original) The anti-CD3 antibody molecule of claim 19, wherein the heavy chain variable region has at least one CDR selected from the group of amino acid sequences of SEQ ID NOs:1, 2, and 3.
22. (Original) The anti-CD3 antibody molecule of claim 20, wherein the light chain variable region has at least one CDR selected from the group of amino acid sequences of SEQ ID NOs:4, 5, and 6.
23. (Original) The anti-CD3 antibody molecule of claim 19, wherein the heavy chain variable framework region has at least one amino acid sequence selected from the group of consisting of SEQ ID NOs:7, 8, 9, and 10.

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24. (Original) The anti-CD3 antibody molecule of claim 19, wherein the light chain variable framework region has at least one amino acid sequence selected from the group of consisting of SEQ ID NOs:11, 12, 13, and 14.

25. (Original) The anti-CD3 antibody molecule of claim 19, wherein the heavy chain variable region has the amino acid sequence shown in SEQ ID NO:17.

26. (Original) The anti-CD3 antibody molecule of claim 19, wherein the light chain variable region has the amino acid sequence shown in SEQ ID NO:15.

27. (Original) The anti-CD3 antibody molecule of claim 19, wherein the light chain variable region is linked to a human type lambda constant region.

28. (Original) The anti-CD3 antibody molecule of claim 19, wherein the heavy chain variable region is linked to a heavy chain constant region of an IgG1 isotype.

29. (Original) The anti-CD3 antibody molecule of claim 19, wherein the heavy chain constant region is aglycosylated.

30. (Original) The anti-CD3 antibody molecule of claim 29, wherein the asparagine residue at position 297 of the constant region is modified.

31. (Original) A pharmaceutical composition comprising the hybrid antibody molecule of either claim 1 or 19, and a pharmaceutically acceptable carrier.

32. (Canceled)

33. (Withdrawn) A method of providing a modified antibody preparation having improved assembly characteristics, comprising:
providing a first nucleic acid encoding a heavy chain variable region selected from the group consisting of:

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(a) a heavy chain variable region at least 95% identical to the heavy chain variable region of a donor immunoglobulin; and

(b) a heavy chain variable region from the donor immunoglobulin;

providing a second nucleic acid encoding a light chain variable region comprising all three CDR's from a donor immunoglobulin and a light chain variable region framework from an acceptor immunoglobulin; and

introducing said first and second nucleic acids into a host cell under conditions that allow expression and assembly of said light and heavy chain variable regions.

34. (Withdrawn) The method of claim 33, wherein the first and second nucleic acids are linked or unlinked.

35. (Withdrawn) The method of claim 33, wherein the host cell is a mammalian cell.

36. (Withdrawn) The method of claim 35, wherein the mammalian cell is selected from the group consisting of a lymphocytic cell line, CHO, COS cells, and a cell from a transgenic animal.

37. - 39. (Canceled)

40. (Previously Presented) A hybrid antibody molecule, comprising:

at least one light chain variable region comprising all three complementarity determining region (CDR's) from a donor immunoglobulin and a light chain variable region framework from an acceptor immunoglobulin, wherein the light chain variable region is a humanized or a CDR-grafted immunoglobulin chain; and

at least one heavy chain variable region selected from the group consisting of:

(a) a heavy chain variable region which is at least 95% identical to the heavy chain variable region of the donor immunoglobulin; and

(b) a heavy chain variable region from the donor immunoglobulin,

wherein the heavy chain variable region is a chimeric chain.

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41. (Previously Presented) The hybrid antibody molecule of claim 14, wherein the CXCR chemokine receptor is selected from the group consisting of CXCR1, CXCR2, CXCR3 and CXCR4.

42. (Previously Presented) The anti-CD3 antibody of claim 26, wherein SEQ ID NO:15 has at least one change selected from the group consisting of:

- a) an Ala at position 2;
- b) a Val at position 4; and
- c) a Leu at position 46.

43. (Previously Presented) The hybrid antibody molecule of claim 11, wherein the light chain constant region is a human type lambda.

44. (New) The hybrid antibody molecule of claim 5, wherein the heavy chain variable region is from a primate.

45. (New) The hybrid antibody molecule of claim 40, wherein the heavy chain variable region is from a primate.

46. (New) The hybrid antibody molecule of claim 45, which comprises a heavy chain constant region of the human IgG1 isotype.

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